

Oral Presentations

Workshop 4. Using registries to identify new challenges

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WS4.5 Cystic fibrosis mutations and survival

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Objective: Show relative survivorship associated with specific disease-causing mutations of the cystic fibrosis (CF) transmembrane conductance regulator (CFTR). **Methods:** We assessed survival effects of CFTR mutations using the CF Foundation Patient Registry (CFFPR). We estimated hazard ratios corrected for age and sex for F508del compound heterozygotes relative to homozygotes.

Results: The CFFPR 1986–2011 records data for 44,989 patients; 29,783 have CFTR mutation information; 48 mutations affect at least 20 patients. There were 9 Class IV or V mutations with better survivorship than F508del: R117H, hazard ratio (HR)=0.22, $p < 0.001$; 2789+5G→A, HR=0.40, $p < 0.001$; D1152H, HR=0.14, $p < 0.001$; A455E, HR=0.36, $p = 0.002$; 3849+10kbC→T, HR=0.56, $p = 0.002$; 5T, HR < 0.01, $p = 0.002$; R347H, HR=0.27, $p = 0.009$; R117C, HR < 0.01, $p = 0.014$; 3272–26A→G, HR=0.24, $p = 0.047$. Two Class I mutations were more severe than F508del: Q493X, HR=1.96, $p = 0.007$ and 3905insT, HR=1.79, $p = 0.03$, and one Class I mutation was less severe: W1282X, HR=0.61, $p = 0.008$. G551D and I507del had survivorship effects similar to F508del.

Conclusions: With a non-overlapping cohort with more complete genotyping, we replicated most prior survivorship results [1]. I507del was no longer distinguishable from F508del; nine other findings were new: seven mutations were milder and two were more severe than F508del. Variable courses of disease associated with mutations of the same class indicate different molecular mechanisms of disease.

Reference(s)

- [1] McKone E, Emerson S, Edwards K, Aitken M. Effect of genotype on phenotype and mortality in cystic fibrosis: a retrospective cohort study. *Lancet* 2003; 361(9370): 1671–1676.

WS4.6 Cancer in patients with cystic fibrosis

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Objectives: Currently almost 8000 people with cystic fibrosis are living in Germany. Due to medical advances, life expectancy of patients with cystic fibrosis has more than doubled in recent years. As a result, the aging patients are affected with diseases of middle age: several of our patients are currently suffering from various neoplasms. This raises the question if there is a relationship between cystic fibrosis and cancer disease.

Methods: For this trial, a prospective data collection was used. Data of Patients with the diagnosis of neoplasm were retrospectively analysed. These data were compared with the risk of suffering from cancer in the age group between 25 and 49 years. For this purpose, the statistics of the German Cancer Registry were used.

Results: At the time of data analyzation 286 patients were documented in march 2013. Of these, 195 are over 18 yrs and 91 under 18 yrs old. 3 male and 9 female were diagnosed with cancer. Compared with the general population (0.93%) female patients with CF between 25 and 49 years of age were more likely to have cancer with 4.32%. In male patients with CF (2.17%), the incidence rate was higher than in the general population (0.56%), too.

Conclusion: In this prospective data collection a difference in the incidence of tumors in patients with CF compared to the general population was evaluated. A relationship between cystic fibrosis and cancer disease is possible. A Germany-wide analysis with an enhanced possibility of documentation in the German documentation system “Muko.dok” and further research is urgently needed. Consequences of these results could be an earlier routine checkup with the aim of detecting cancer.